REMARKS

Response to Issues Raised in Notice of Non-Compliant Amendment

Status of Claim 122

The Notice objected to claim 122 as reciting the incorrect status. However, Applicants believe claim 122 is withdrawn correctly. In the Office Action mailed August 22, 2008, claim 122 was objected to for depending on claim 121, which is withdrawn as non-elected. Claim 121 became withdrawn following Applicants election on May 12, 2008 of species (a) in response to the restriction requirement mailed December 11, 2007. Species (a) is drawn to "a polypeptide comprising S polypeptide SEQ ID NO:6042, a fragment thereof, and fusion peptide comprising a tag sequence." Restriction Requirement at page 2. As noted in Applicants May 12, 2008 response to the restriction requirement, claims 1-8, 22, 23, 25, 26 94-98, 114, 115, and 117 read on species (a). Claim 121 recites the polypeptide of claim 8 with a second SARS virus protein or a fragment. Claim 122 recites particular fragments. The restriction requirement placed both these claims into species (b), which Applicants did not elect. Thus, based on the restriction requirement issued by the Office, Applicants believe claim 122 is correctly withdrawn.

Request to Identify Provisional Application Disclosing SEQ ID NO:7307

The Notice also requests that Applicants identify the provisional application that discloses SEQ ID NO:7307.[1] The M.P.E.P. states that "[a] requirement for information necessary for finding prior art is not a substitute for the examiner performing a search of

[1] Applicants note that SEQ ID NO:7307 is under examination, rather than SEQ ID NO:7302 as stated in the Notice.

the relevant prior art; the examiner must make a search of the art according to MPEP § 704.01 and §§ 904-904.03." M.P.E.P § 704.11. The Patent Office already has the sequence data corresponding to SEQ ID NO:7307 and is therefore able to search for and apply prior art. Nevertheless, in the interests of compact prosecution, Applicants have reviewed the provisional applications and identified No. 60/468,312, filed May 22, 2003 as disclosing SEQ ID NO:7307. Specifically, page 140 teaches residues 14-662 of SEQ ID NO: 147. SEQ ID NO: 147 is, as noted *infra*, the same sequence as SEQ ID:6042. Residues 14-662 of SEQ ID:6042 are identical to SEQ ID NO:7307.

Amendments to the Specification

The specification is amended to delete hypertext links and correct trademark usage.

Amendments to the claims

Claim 94's recitation that the peptide is isolated is supported throughout the specification; at page 29, line 3 to page 31, line 33, for example. Claim 96's recitation of a transmembrane domain is supported, *inter alia*, at page 29, lines 22-24. Claim 114 is amended to depend from claim 23. Claim 2 is amended to correct a clerical error. New claims 127 and 128 are supported, *inter alia*, at page 297, line 21 to page 299, line 1. New claims 129-132 are supported, *inter alia*, at page 30, line 1 to page 31, lines 15-25.

Claim Objections

Claim 96 and 122 stand objected for informalities. Claim 96 is amended to recite a transmembrane domain region and claim 122 is now withdrawn.

Applicants respectfully request withdrawal of the objections.

Rejection Under 35 U.S.C. § 101

Claims 94-98 stand rejected as directed to non-statutory subject matter. Claim 94 is amended to recite an isolated polypeptide. Claims 95-98 depend from claim 94. The claims are no longer directed to products of nature.

Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 112

Claims 22, 23, 25-28, 114, 115, and 117 stand rejected as not enabled because undue experimentation would be required to develop a SARS vaccine.

Applicants respectfully traverse the rejection.

A patent specification must teach a person skilled in the relevant art how to make and use the invention claimed. 35 U.S.C. § 112 ¶ 1. The legal test for whether a disclosure provides adequate enablement for a generic claim is that "the scope of the claims must bear a *reasonable correlation* to the scope of enablement provided by the specification to persons of ordinary skill in the art." *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970) (emphasis added), *cited with approval in Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1212, 18 U.S.P.Q.2d 1016, 1026 (Fed. Cir. 1991). The standard for determining whether the present specification meets the enablement requirement is whether any experimentation which may be needed to practice the invention is undue. *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). Even complex experimentation may not be considered undue if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221

U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774, F.2d 1104 (Fed. Cir. 1985). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463 (Fed. Cir. 1984).

The Office Action at page 6 acknowledges that the specification discloses how to makes polypeptides and subunit S polypeptides. The Office Action also acknowledges that Examples 4 and 5 of the specification teach that inactivated SARS vaccine can induce neutralizing antibodies in mice and Balb/c mice. *Id.* Nevertheless, the Office Action contends, citing Weiss,[2] that the "mice model is not [an] art-recognized animal model for assessing SARS infection." *Id.*

Whether an animal model accurately reproduces a disease etiology is not the test of whether the animal model correlates to the condition. Citing *In re Brana*, 51. F.3d 1560, 1566 (Fed. Cir. 1995), the M.P.E.P. explains that:

> …[i]f the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate.

M.P.E.P § 2164.02. Thus, a rigorous or invariable exact correlation is not required. *Cross. v. Iisuka*, 753 F.2d 1040 (Fed. Cir. 1985).

Weiss may teach that the mouse is not a perfect model for understanding SARS *pathology*; however, Weiss demonstrates clearly that the art recognizes, and continues to use, mice models to test SARS vaccines. Weiss acknowledges issues using animal

[2] Weiss SR, Navas-Martin S. "Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus," Microbiol Mol Biol Rev. 2005 Dec;69(4):635-64. Weiss was published after Applicants' filing date.

models for SARS disease. See page 653, col.2 ¶ 3. But Weiss recognizes that mice models are used for testing SARS vaccines: "It should be emphasized that these animals (in particular mice and macaques) are currently being exploited for vaccine studies." Page 653, col.2 ¶ 3. Weiss also describes multiple SARS vaccine studies using experiments performed in mice, including at least one study demonstrating protection from SARS: "[A] DNA vaccine encoding the codon-optimized SARS spike glycoprotein induces neutralizing antibody as well as T-cell responses. Protection from SARS-CoV challenge was mediated by a humoral immune response but not by a T-cell dependent mechanism." See Page 654, col.1 ¶ 3. Thus, Weiss recognizes that the mouse model is art-recognized for SARS vaccine research.

The Office Action also considers the claims lack enablement because "the molecular biology and pathogenesis of SARS-HCoV were largely unknown" and, citing Stockman,[3] because "the prior art indicates that no drug or treatment has been proven to be effective for control of SARS." Office Action at page 7. Neither rationale supports a lack of enablement. First, vaccine development does not require that the molecular biology and pathogenesis of SARS virus is known. Indeed, as discussed above, the skilled artisan performs vaccine studies in mice, which may not be a good model for understanding either SARS virus molecular biology or pathology, but is useful in vaccine research. Second, Stockman describes the failure of ribavirin, lopinavir, corticosteroids, interferon, intravenous immunoglobulin and convalescent plasma to treat SARS. However, Stockman teaches nothing about vaccine-based treatments using the host's immune system. Thus, nothing in Stockman suggests that Applicants claimed subject

[3] Stockman LJ, Bellamy R, Garner P., "SARS: systematic review of treatment effects," PLoS Med. 2006 Sep;3(9):e343

matter is not enabled.

Finally, the Office action suggests that if SARS virus reemerges in humans, its spike protein might not be the same and thus Applicants' vaccine might not be effective. Office Action at page 7. This is speculation based on Cavanagh's statement that the "S1 protein might not be the same as that of the 2002/2003 outbreak. Research with IBV [Infectious Bronchitis Virus] has indicated that differences of only 5% of S1 protein amino acid can reduce cross-protection." Page 577, col.2 ¶ 4. But nothing in Cavanagh shows that Applicants vaccine will not protect against a hypothetical future SARS variant. Indeed, there is nothing in Cavanagh to suggest that that SARS virus even mutates as IBV does. IBV is a type 3 coronavirus and SARS virus has been classed as a Group 4 coronavirus because of "extremely low amino acid identity between its proteins and those of the other three groups, and [the] nature and organization of its non-structural protein genes." Page 568, col.2. Table 1 legend. Finally, rather than suggesting that the S1 protein will not be useful as a vaccine, Cavanagh *encourages* using the S1 protein in SARS vaccines: "Looking further into the future, the high efficacy of the fowl adenovirus vector expressing the IBV S1 subunit provides optimism for a live SARS vaccine." Abstract, p.568. Nothing in Cavanagh provides any reason to doubt Applicants' claims are enabled.

The experimentation required to develop a SARS vaccine may be complex but it is not undue. The specification provides detailed instructions how to prepare spike glycoprotein; how to perform the mouse experiments; and provides examples with inactivated virus detailing the neutralizing antibody response obtained in mice, an accepted model for identifying SARS vaccines. Weiss demonstrates that Applicants'

disclosed experiments are regularly performed in the art. The weight of the evidence establishes that claims 22, 23, 25-28, 114, 115, and 117 are enabled. The Office Action has not established a *prima facie* case to the contrary.

Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102

Claims 1-8, 22, 23, 27, 28, and 94 stand rejected under 35 U.S.C. § 102(e) as anticipated by Plummer (US2007/0258999) as evidenced by Dimitrov (US2006/0240515A1).

Applicants respectfully traverse the rejection.

Plummer's spike protein sequence is not prior art to Applicants spike sequence because Applicants were in possession of Plummer's disclosed Spike sequence prior to Plummer's filing date. See *In re Stempel*, 241 F.2d 755, 759 (CCPA 1957)(Holding that "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference.")

Plummer's only disclosed Spike sequence is SEQ ID NO:33, which is identical to Applicants SEQ ID NO:6042. Applicants claim priority to U.S. provisional application No. 60/463109, filed April 14, 2003. SEQ ID NO:147[4] in Application No. 60/463109 discloses the identical sequence to SEQ ID NO:6042. Applicants' invention thus pre-dates Plummer, which has an earliest possible filing date of April 28, 2003. Thus, while the sequence identifier "6042" may have been used for the first time in Application Serial

[4] Copies of Provisional Application 60/463,109 pages 42 to 48, which disclose SEQ ID NO:6042 as SEQ ID: 147, are enclosed as Exhibit 1 for the Examiner's convenience.

No. 60/51781, filed October 11, 2003 (noted at page 3 of the Office Action), the sequence itself was first disclosed as sequence identifier 147 in Application Serial 60/463109, filed April 14, 2003. Plummer is therefore not prior art to SEQ ID NO:6042 or SEQ ID NO:7307.

Applicants respectfully request withdrawal of the rejection.

Rejections Under 35 U.S.C. § 103(a)

Claims 95-98 stand rejected under 35 U.S.C. § 103(a) as obvious over Plummer and Cavanagh *et al*. (J. Gen. Virol. 1986 67:1435-42; "Cavanagh"). Claims 25, 26, 114, 115, and 117 stand rejected under 35 U.S.C. § 103(a) as obvious over Plummer and Gasparini *et al*. (Eu. J. Epidemiol. 2001 17:135-140; "Gasparini.")

Plummer is cited as teaching SEQ ID NO:33, the Spike protein, prior to Applicant's priority date. As discussed above, Plummer's teaching of SEQ ID NO:33 is not prior art to SEQ ID NO:6042 or SEQ ID NO:7307. Neither Cavanagh nor Gasparini cures the deficiency of Plummer. The Office Action has not established a *prima facie* case of obviousness.

Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

BANNER & WITCOFF, LTD.

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Customer No. 22907

By: /Dale H. Hoscheit/
Dale H. Hoscheit
Registration No. 19,090